

**REMARKS****INTRODUCTION:**

In accordance with the foregoing, claims 13 and 24 have been amended. No new matter is being presented, and approval and entry are respectfully requested.

Claims 13-15 and 24-26 are pending and under consideration. Reconsideration is respectfully requested.

**REJECTION UNDER 35 U.S.C. §112:**

In the Office Action, at pages 2-4, numbered paragraph 2, claims 13-15 and 24-26 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is traversed and reconsideration is requested.

For clarity, independent claims 13 and 24 have been amended. These amendments are supported, for example, by page 1, lines 9-17, page 7, lines 10-19, page 27, line 35 through page 28, line 4, page 43, lines 5-31 of the specification, and the Abstract.

It may be helpful to describe the environment of the implementation of the present invention. Those skilled in the art know that biological data reflects differences, even within similar data. In mathematical data, such differences may be termed "outliers." Scientists review data and attempt to organize it into meaningful form, despite the differences, to determine general relationships.

As noted in Merriam Webster's On-line dictionary, a "function" refers to "the action for which a person or thing is especially fitted or used or for which a thing exists." That is, as utilized in the specification of the present invention, a "function" refers to the action for which a thing (a sequence of atoms) is especially fitted or for which the sequence of atoms exists.

It is often of interest to identify regions of a protein that are responsible for specific properties.

As stated in USPN 6,238,884, col. 2, lines 55-64: "The complexity of an active sequence of a biological macromolecule (e.g., polynucleotides, polypeptides, and molecules that are comprised of both polynucleotide and polypeptide sequences) has been called its information content ("IC"), which has been defined as the resistance of the active protein to amino acid sequence variation (calculated from the minimum number of invariable amino acids (bits) required to describe a family of related sequences with the same *function*). Proteins that are

more sensitive to random mutagenesis have a high information content.”

As recited at <http://www.pubmedcentral.nih.gov/botrender.fegi?blobtype=html&artid=517493> in Automatic annotation of protein motif function with Gene Ontology terms by Xinghua Lu, Chengxiang Zhai, Vanathi Gopalokrishnan and Bruce G. Buchanan, BMC Bioinformatics, 2004, 5:122: “Conserved protein sequence motifs are short stretches of amino acid sequence patterns that potentially encode the function of proteins. Several sequence pattern searching algorithms and programs exist for identifying candidate protein motifs at the whole genome level. With the completion of many genome sequencing projects and advances in the methods of automatic discovery of sequence patterns, it is now possible to search or discover protein sequence motifs at the genome level. If one regards protein sequences as “sentences” of the biological language with amino acids as the alphabet, then protein motifs can be considered as words or phrases of that language and determining the function of a motif is equivalent to determining the sense of a word. Identifying biological sequence motifs has been a fundamental task of bioinformatics, which has led to the development of several motif (pattern) databases, such as PROSITE, BLOCKS, SMART and Pfam [3-6]. These databases are usually constructed by studying the set of protein sequences that are known to have certain functions and extracting the conserved sequence motifs that are believed to be responsible for their functions.”

Hence, it is respectfully submitted that in the biological environment of the present claimed invention, the terminology “function of “sequences of atoms” or of “atomic groups” is understood by one skilled in the art. The “standard” for ascertaining the meaning of the term “function” has been determined by those skilled in the art and utilized to generate databases for protein sequences, amino acid sequences, and groups of atoms that are known to have certain functions. The present invention makes use of such databases in determining a presence of amino acid sequences of protein molecules that correlate with said databases.

Reference databases are known to those skilled in the art. For example, as noted in lines 21-28 of page 3 of the specification: “As a typical data base, a PDS (Protein Data Bank) in which three-dimensional structures of proteins or the like identified by the X-ray crystal analysis of protein are registered is widely known and universally used. Further, a CSD (Cambridge Structural Database) is known as a data base in which chemical substances are registered.”

Independent claim 13, and independent claim 24 in similar fashion has been amended to recite “A method of analyzing, by a computer, three-dimensional structures of amino acid sequences of ~~atoms or atomic groups of~~ protein molecules of biological substances including a first structure of ~~a-an amino acid sequence of atoms or an atomic group of a~~ protein molecule of a probe first biological substance expressed by three-dimensional coordinates of elements

belonging to a first point set and a second structure of ~~a~~an amino acid ~~sequence of atoms or an atomic group of a~~ protein molecule of a target second biological substance expressed by three-dimensional coordinates of elements belonging to a second point set..." As such, it is respectfully submitted that the Examiner's example does not clearly recite an amino acid sequence of a protein molecule, and hence does not apply to amended independent claims 13 and/or 24.

Similarly, it is respectfully submitted that, in view of the amendments to independent claims 13 and 24, the Examiner's recitation "For example, if 3-D coordinates of a phosphate group (i.e., "atomic group") in a nucleic acid correlates with a 3-D coordinates of a phosphate group in a lipid or a protein, what kind of function is determined to be "substantially equivalent" does not apply. Similarly, the Examiner's question: "What function will be understood, e.g., for a sequence of C-C-C-N atoms?" does not apply to amended independent claims 13 and 24.

Hence, it is respectfully submitted that the terminology "function" is defined and standardized by those skilled in the art who prepare the reference databases that list functions that correlate with specific amino acid sequences that are selected to be utilized. For example, PDS (Protein Data Bank), in which three-dimensional structures of proteins or the like are identified by the X-ray crystal analysis of protein (see above reference), recites at [http://function.rcsb.org:8080/pdb/function\\_distribution/index.html](http://function.rcsb.org:8080/pdb/function_distribution/index.html): "Functional Distributions This site provides the structural genomics community a resource to choose suitable targets and is intended for continuously quantifying the bias of protein structure and function."

The terminology "for a sequence of atoms" or for "a sequence of atomic groups" is submitted to be known to those skilled in the art with respect to protein molecules. However, in view of the amendments to claims 13 and 24, the concerns about such terminology are now moot.

It is respectfully submitted that, for example, scientists have determined structures that have shown heat resistance and have made databases for same.

Hence, it is respectfully submitted that amended independent claims 13 and 24 are definite under 35 U.S.C. §112, second paragraph, and particularly point out, and distinctly claim the subject matter which applicant regards as the invention.

#### **REJECTION UNDER 35 U.S.C. §101:**

In the Office Action, at pages 4-6, numbered paragraph 3, claims 13-15 and 24-26 were rejected under 35 U.S.C. §101 because the Examiner submitted that the invention lacks patentable utility. This rejection is traversed and reconsideration is requested.

Independent claims 13 and 24 have been amended for clarity (see above).

It is respectfully submitted that amended independent claim 13, and independent claim 24 in similar fashion, recites a method of analyzing, by a computer processor, three-dimensional structures of amino acid sequences of atoms or atomic groups of protein molecules of biological substances, including a first structure of an amino acid sequence of a protein molecule of a probe first biological substance expressed by three-dimensional coordinates of elements belonging to a first point set and a second structure of an amino acid sequence of a protein molecule of a target second biological substance expressed by three-dimensional coordinates of elements belonging to a second point set.... outputting, to a display unit, a superposed display of a three-dimensional structure of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance expressed by three-dimensional coordinates of elements belonging to the first point set and the second structure of the amino acid sequence of the protein molecule of the target second biological substance and a determination, if the degree of spatial similarity between the first structure of the amino acid sequence of the protein molecule of the probe first biological substance and the second structure of the amino acid sequence of the protein molecule of the target second biological substance is greater than or equal to the predetermined threshold degree of similarity, that a function of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance is substantially equivalent to a function of the second structure of the amino acid sequence of the protein molecule of the target second biological substance.

As described more fully above, databases are available which are utilized by those skilled in the art to correlate protein molecule function with structure. Thus, upon correlating a structure of a probe first biological substance with a structure of a target second biological substance, the function of the target second biological substance is ascribed to the probe first biological substance. Hence, it is respectfully submitted that the present claimed invention is a useful invention and the usefulness is immediately apparent to those familiar with the technological field of the invention.

Amended independent claims 13 and 24 output a superposed display of a three-dimensional structure of the first structure of the sequence of atoms or the atomic group of the protein molecule of the probe first biological substance expressed by three-dimensional coordinates of elements belonging to the first point set and the second structure of the sequence

Thus, it is respectfully submitted that amended independent claims 13 and 24 have patentable utility and are patentable under 35 U.S.C. §101. Since claims 14-15 and 25-26 depend from amended independent claims 13 and 24, respectively, claims 14-15 and 25-26 have patentable utility and are patentable under 35 U.S.C. §101 for at least the reasons amended independent claims 13 and 24 have patentable utility and are patentable under

35 U.S.C. §101.

**REJECTION UNDER 35 U.S.C. §112:**

In the Office Action, at page 6, numbered paragraph 4, claims 13-15 and 24-26 were rejected under 35 U.S.C. §112, first paragraph, because the Examiner submits that said claims are not supported by a substantial and credible asserted utility or a well established utility and that one skilled in the art would clearly not know how to use the claimed invention. This rejection is traversed and reconsideration is requested.

Independent claims 13 and 24 have been amended for clarity (see above).

It is respectfully submitted that, as amended, independent claim 13, and similarly, independent claim 24, has a credible asserted utility of a method of analyzing, by a computer processor, three-dimensional structures of amino acid sequences of protein molecules of biological substances, including a first structure of an amino acid sequence of a protein molecule of a probe first biological substance expressed by three-dimensional coordinates of elements belonging to a first point set and a second structure of an amino acid sequence of a protein molecule of a target second biological substance expressed by three-dimensional coordinates of elements belonging to a second point set.... outputting, to a display unit, a superposed display of a three-dimensional structure of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance expressed by three-dimensional coordinates of elements belonging to the first point set and the second structure of the amino acid sequence of the protein molecule of the target second biological substance and a determination, if the degree of spatial similarity between the first structure of the amino acid sequence of the protein molecule of the probe first biological substance and the second structure of the amino acid sequence of the protein molecule of the target second biological substance is greater than or equal to the predetermined threshold degree of similarity, that a function of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance is substantially equivalent to a function of the second structure of the amino acid sequence of the protein molecule of the target second biological substance.

It is respectfully submitted that the method of the present invention, as set forth in amended independent claims 13 and 15, is clear to one skilled in the art. Thus, amended independent claims 13 and 15 are respectfully submitted to be in patentable form under 35 U.S.C. §112, first paragraph. Since claims 14-15 and 25-26 depend from amended independent claims 13 and 24, respectively, claims 14-15 and 25-26 are submitted to be in patentable form under 35 U.S.C. §112, first paragraph for at least the reasons amended independent claims 13 and 24 are in patentable form under 35 U.S.C. §112, first paragraph.

**REJECTION UNDER 35 U.S.C. §101:**

In the Office Action, at pages 6-8, numbered paragraph 5, claims 13-15 and 24-26 were rejected under 35 U.S.C. §101 because the Examiner submitted that the claimed invention is directed to non-statutory subject matter. This rejection is traversed and reconsideration is requested.

It is respectfully submitted that amended independent claim 13, and independent claim 24 in similar fashion, recites a method of analyzing, by a computer processor, three-dimensional structures of amino acid sequences of atoms or atomic groups of protein molecules of biological substances, including a first structure of an amino acid sequence of a protein molecule of a probe first biological substance expressed by three-dimensional coordinates of elements belonging to a first point set and a second structure of an amino acid sequence of a protein molecule of a target second biological substance expressed by three-dimensional coordinates of elements belonging to a second point set.... outputting, to a display unit, a superposed display of a three-dimensional structure of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance expressed by three-dimensional coordinates of elements belonging to the first point set and the second structure of the amino acid sequence of the protein molecule of the target second biological substance and a determination, if the degree of spatial similarity between the first structure of the amino acid sequence of the protein molecule of the probe first biological substance and the second structure of the amino acid sequence of the protein molecule of the target second biological substance is greater than or equal to the predetermined threshold degree of similarity, that a function of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance is substantially equivalent to a function of the second structure of the amino acid sequence of the protein molecule of the target second biological substance.

As described more fully above, databases are available which are utilized by those skilled in the art to correlate protein molecule function with structure. Thus, upon correlating a structure of a probe first biological substance with a structure of a target second biological substance, the function of the target second biological substance is ascribed to the probe first biological substance. Hence, it is respectfully submitted that the present claimed invention is directed to statutory subject matter.

The terminology "function" and how function is determined is described above.

Independent claims 13 and 24 have been amended for clarity (see above). It is respectfully submitted that amended independent claims 13 and 24 are not broader than the statutory embodiments of the claims.

Amended independent claims 13 and 24 recite outputting to a display unit. Hence, it is respectfully submitted that a tangible real-world result is obtained.

Thus, amended independent claims 13 and 24 are submitted to be directed to statutory subject matter and to be allowable under 35 U.S.C. §101. Since claims 14-15 and 25-26 depend from amended independent claims 13 and 24, claims 14-15 and 25-26 are directed to statutory subject matter and are allowable under 35 U.S.C. §101 for at least the reasons amended independent claims 13 and 24 are directed to statutory subject matter and are allowable under 35 U.S.C. §101.

### **REJECTION UNDER 35 U.S.C. §102:**

In the Office Action, at pages 8-10, numbered paragraph 6, claims 13-15 and 24-26 were rejected under 35 U.S.C. §102(b) as being anticipated by Flaherty et al. (Proc. Natl. Acad. Sci. USA, 88, 5041-5045, 1991) or Mosimann et al. The rejection is traversed and reconsideration is requested.

Independent claims 13 and 24 have been amended for clarity (see above).

Amended independent claims 13 and 24 include the operation of outputting, to a display unit, a superposed display of a three-dimensional structure of the first structure of the amino acid sequence of the protein molecule of the probe first biological substance expressed by three-dimensional coordinates of elements belonging to the first point set and the second structure of the amino acid sequence of the protein molecule of the target second biological substance.

It is respectfully submitted that Flaherty teaches a process of initially superimposing the examined structure and comparison structure, inspecting by eye and guiding the classification of C<sub>α</sub> positions into equivalent corresponding atoms in aligned α-helices and β-strands, versus non-equivalent, such as those in loops that traverse different routs or are of different lengths. Then additional stretches of equivalent polypeptide chains were then identified and included in the optimal superposition between the two molecules. Then visual inspection was required to determine at which residue the backbones diverge. That is, empirical identification of equivalent residues was used in preference to computational methods that rely primarily on distance criteria (see col. 2, page 5041, Flaherty). It is respectfully submitted that visual inspection and empirical adjustment of superposition not based on calculation, as is recited in Flaherty, is different from the calculation operations utilized in the present claimed invention. Hence, it is respectfully submitted that amended independent claims 13 and 24 of the present invention are not anticipated under 35 U.S.C. §102(b) by Flaherty et al. (Proc. Natl. Acad. Sci. USA, 88, 5041-5045, 1991). Since claims 14-15 and 25-26 depend from amended independent claims 13 and 24, respectively, claims 14-15 and 25-26 are not anticipated under 35 U.S.C. §102(b) by

Flaherty et al. (Proc. Natl. Acad. Sci. USA, 88, 5041-5045, 1991) for at least the reasons amended independent claims 13 and 24 are not anticipated under 35 U.S.C. §102(b) by Flaherty et al. (Proc. Natl. Acad. Sci. USA, 88, 5041-5045, 1991).

It is respectfully submitted that Mosimann teaches a two step procedure that requires a revision of the alignment based on inspection of the examined sequence fitted into the selected structure. Hence, Mosimann teaches away from the present claimed invention, which does not require a revision of the alignment based on inspection of the examined sequence fitted into the comparison structure. Thus, it is respectfully submitted that amended independent claims 13 and 24 are not anticipated under 35 U.S.C. §102(b) by Mosimann et al. Since claims 14-15 and 25-26 depend from amended independent claims 13 and 24, respectively, claims 14-15 and 25-26 are not anticipated under 35 U.S.C. §102(b) by Mosimann et al. for at least the reasons amended independent claims 13 and 24 are not anticipated under 35 U.S.C. §102(b) by Mosimann et al.

#### **DOUBLE PATENTING:**

In the Office Action, at page 10, numbered paragraph 7, claims 13-15 and 24-26 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16, 17 of co-pending application 09/909,809 or claims 5-11, 24 of co-pending application 09/910,054.

It is respectfully submitted that Applicants did not submit that the rejection was premature. Instead, the Applicants submitted, and continue to submit that any submission of a Terminal Disclaimer or arguments as to the non-obvious nature of the claims would be premature because U.S. Patent Application Nos. 09/909,809 and 09/910,054 have not yet been issued as patents, and all of the claims of the instant application have not yet been indicated as allowable except for the provisional rejection.

Hence, Applicants respectfully request that the Applicants be allowed to address any obviousness-type double patenting issues remaining once the rejections of the claims of the present claimed invention are resolved or on allowance of U.S. Patent Application Nos. 09/909,809 and/or 09/910,054.

#### **CONCLUSION:**

In accordance with the foregoing, it is respectfully submitted that all outstanding objections and rejections have been overcome and/or rendered moot. And further, that all pending claims patentably distinguish over the prior art. Thus, there being no further outstanding objections or rejections, the application is submitted as being in condition for allowance which action is earnestly solicited.



If the Examiner has any remaining issues to be addressed, it is believed that prosecution can be expedited by the Examiner contacting the undersigned attorney for a telephone interview to discuss resolution of such issues.

If there are any underpayments or overpayments of fees associated with the filing of this Amendment, please charge and/or credit the same to our Deposit Account No. 19-3935.

Respectfully submitted,

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